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## Arrhythmias and Clinical EP

**VIRAL ANTI-INFLAMMATORY PROTEIN TREATMENT SIGNIFICANTLY ALTERS GENE EXPRESSION IN CIRCULATING LEUKOCYTES FROM PATIENTS AFTER ATRIAL FIBRILLATION CRYOBALLOON ABLATION**

Poster Contributions

Hall C

Sunday, March 30, 2014, 9:45 a.m.-10:30 a.m.

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**Background:** Cryoballoon ablation (CB) for atrial fibrillation (AF) activates inflammation that may lead to increased atrial fibrosis, thrombosis, and recurrent arrhythmia. Two viral anti-inflammatory proteins, M-T7 (a chemokine/glycosaminoglycan inhibitor) and Serp-1 (a serine protease inhibitor) have proven anti-inflammatory activity in animal models. Serp-1 also reduced markers of myocardial damage in patients after coronary stent implant. In this study, we examined the systemic inflammatory response to AF ablation and the potential to modify inflammatory cell activation after ablation using these viral proteins.

**Methods:** Fifteen patients were studied after CB or CB with radiofrequency ablation. White blood cells (WBCs) were isolated for analysis and treatment with the anti-inflammatory viral proteins ex vivo. Serum markers of inflammation and myocardial injury were measured pre and post ablation.

**Results:** Troponin, WBC, high-sensitivity C-reactive protein, and Fibrinogen demonstrated significant increases in mean levels 24 hours after ablation (1.55 ng/L, 17.82 mg/L, 3.21 cells/ $\mu$ L and 38.32 mg/dL, respectively,  $P < 0.001$  for each). Isolated leukocytes from venous samples showed increased cell activation confirmed by membrane fluidity analysis using a fluorescent Bispyrenylpyrene assay ( $P < 0.001$ ). RT-PCR array analysis detected a 4.8 fold increase in caspase recruitment domain 8 genes (CARD8) in cells exposed to M-T7. In addition, MT7 down-regulated caspase 8 and 9 gene expression relative quantity (RQ) to 0.006 and 0.2, respectively ( $P < 0.008$  for each), while Serp-1 down-regulated tumor necrosis RQ to 0.45 ( $P < 0.005$ ), and p53 to 0.36023 ( $P = 0.009$ ). Reductions were also detected in caspases 8 and 9 (RQ - 0.0015 for each;  $P < 0.0068$ ).

**Conclusions:** Circulating blood leukocytes isolated from patients after CB for atrial fibrillation demonstrate increased cellular activation. Treatment of these cells with viral anti-inflammatory proteins significantly reduces activation and selectively modifies apoptotic pathway gene expression.